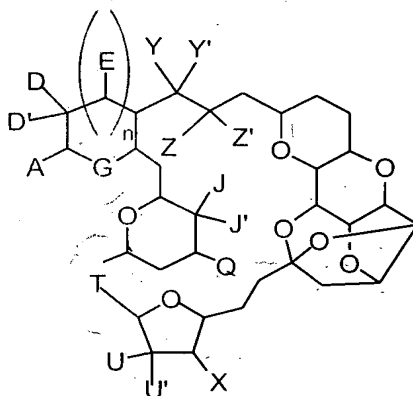


CLAIMS

1. A compound having the formula:



wherein A is a C₁₋₆ saturated or C₂₋₆ unsaturated hydrocarbon skeleton, said skeleton being unsubstituted or having between 1 and 10 substituents, inclusive, independently selected from cyano, halo, azido, oxo, and Q₁;

each Q₁ is independently selected from OR₁, SR₁, SO₂R₁, OSO₂R₁, NR₂R₁, NR₂(CO)R₁, NR₂(CO)(CO)R₁, NR₄(CO)NR₂R₁, NR₂(CO)OR₁, (CO)OR₁, O(CO)R₁, (CO)NR₂R₁, and O(CO)NR₂R₁;

each of R₁, R₂, R₄, R₅, and R₆ is independently selected from H, C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₁₋₆ hydroxyalkyl, C₁₋₆ aminoalkyl, C₆₋₁₀ aryl, C₆₋₁₀ haloaryl, C₆₋₁₀ hydroxyaryl, C₁₋₃ alkoxy-C₆ aryl, C₆₋₁₀ aryl-C₁₋₆ alkyl, C₁₋₆ alkyl-C₆₋₁₀ aryl, C₆₋₁₀ haloaryl-C₁₋₆ alkyl, C₁₋₆ alkyl-C₆₋₁₀ haloaryl, (C₁₋₃ alkoxy-C₆ aryl)-C₁₋₃ alkyl, C₂₋₉ heterocyclic radical, C₂₋₉ heterocyclic radical-C₁₋₆ alkyl, C₂₋₉ hydroxyheterocyclic radical, C₂₋₉ heterocyclic radical-C₁₋₃ alkylhydroxy, C₂₋₉ heteroaryl, and C₂₋₉ heteroaryl-C₁₋₆ alkyl;

each of D and D' is independently selected from R₃ and OR₃, wherein R₃ is H, C₁₋₃ alkyl, or C₁₋₃ haloalkyl;

n is 0 or 1;

E is R₅ or OR₅;

G is O, S, CH₂, or NR₆;

each of J and J' is independently H, C₁₋₆ alkoxy, or C₁₋₆ alkyl; or J and J' taken together are =CH₂ or -O-(straight or branched C₁₋₅ alkylene)-O-;

Q is C₁₋₃ alkyl;

T is ethylene or ethenylene, optionally substituted with (CO)OR₇, where R₇ is H or C₁₋₆ alkyl;

each of U and U' is independently H, C₁₋₆ alkoxy, or C₁₋₆ alkyl; or U and U' taken together are =CH₂ or -O-(straight or branched C₁₋₅ alkylene)-O-;

X is H or C₁₋₆ alkoxy;

each of Y and Y' is independently H or C₁₋₆ alkoxy; or Y and Y' taken together are =O, =CH₂, or -O-(straight or branched C₁₋₅ alkylene)-O-; and

each of Z and Z' is independently H or C₁₋₆ alkoxy; or Z and Z' taken together are =O,

=CH₂, or -O-(straight or branched C₁₋₅ alkylene)-O-;
or a pharmaceutically acceptable salt thereof.

2. The compound of claim 1, wherein n is 0.

3. The compound of claim 1, wherein each of D and D' is independently selected from R₃, C₁₋₃ alkoxy, and C₁₋₃ haloalkyloxy.

4. The compound of claim 1, wherein R₅ is selected from H, C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₁₋₆ hydroxyalkyl, C₁₋₆ aminoalkyl, C₆₋₁₀ aryl, C₆₋₁₀ haloaryl, C₆₋₁₀ hydroxyaryl, C₁₋₃ alkoxy-C₆ aryl, C₆₋₁₀ aryl-C₁₋₆ alkyl, C₁₋₆ alkyl-C₆₋₁₀ aryl, C₆₋₁₀ haloaryl-C₁₋₆ alkyl, C₁₋₆ alkyl-C₆₋₁₀ haloaryl, (C₁₋₃ alkoxy-C₆ aryl)-C₁₋₃ alkyl, C_{2,9} heterocyclic radical, C_{2,9} heterocyclic radical-C₁₋₆ alkyl, C_{2,9} heteroaryl, and C_{2,9} heteroaryl-C₁₋₆ alkyl.

5. The compound of claim 1, wherein A comprises a C₁₋₆ saturated or C₂₋₆ unsaturated hydrocarbon skeleton, said skeleton having at least one substituent selected from cyano, halo, azido, oxo, and Q₁;

each Q₁ is independently selected from OR₁, SR₁, SO₂R₁, OSO₂R₁, NR₂R₁, NR₂(CO)R₁, and O(CO)NR₂R₁;

n is 0;

G is O;

J and J' taken together are =CH₂;

Q is methyl;

T is ethylene;

U and U' taken together are =CH₂;

X is H;

each of Y and Y' is H; and

Z and Z' taken together are =O or =CH₂.

6. The compound of claim 1, wherein each Q₁ is independently selected from OR₁, SR₁, SO₂R₁, OSO₂R₁, NH(CO)R₁, NH(CO)(CO)R₁, and O(CO)NHR₁;

each R₁ is independently selected from C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₆ aryl, C₆ haloaryl, C₁₋₃ alkoxy-C₆ aryl, C₆ aryl-C₁₋₃ alkyl, C₁₋₃ alkyl-C₆ aryl, C₆ haloaryl-C₁₋₃ alkyl, C₁₋₃ alkyl-C₆ haloaryl, (C₁₋₃ alkoxy-C₆ aryl)-C₁₋₃ alkyl, C_{2,9} heterocyclic radical, C_{2,9} heteroaryl, and C_{2,9} heteroaryl-C₁₋₆ alkyl;

one of D and D' is methyl or methoxy, and the other is H;

n is 0;

G is O;

J and J' taken together are =CH₂;

Q is methyl;

T is ethylene;
U and U' taken together are =CH₂ ;
X is H;
each of Y and Y' is H; and
Z and Z' taken together are =O.

7. The compound of claim 6, wherein A has at least one substituent selected from hydroxyl, amino, azido, halo, and oxo.

8. The compound of claim 7, wherein A comprises a saturated hydrocarbon skeleton having at least one substituent selected from hydroxyl, amino and azido.

9. The compound of claim 8, wherein A has at least two substituents independently selected from hydroxyl, amino, and azido.

10. The compound of claim 8, wherein A has at least two substituents independently selected from hydroxyl and amino.

11. The compound of claim 8, wherein A has at least one hydroxyl substituent and at least one amino substituent.

12. The compound of claim 8, wherein A has at least two hydroxyl substituents.

13. The compound of claim 8, wherein A comprises a C₂₋₄ hydrocarbon skeleton.

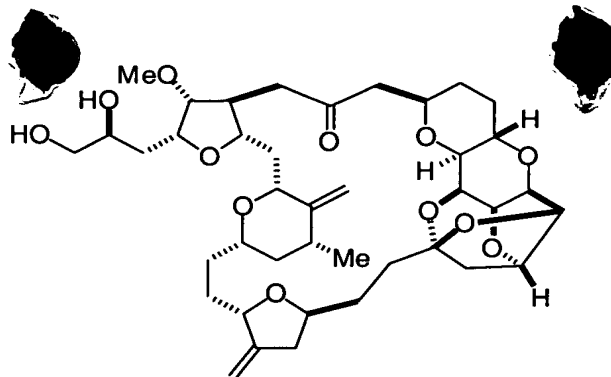
14. The compound of claim 8, wherein A comprises a C₃ hydrocarbon skeleton.

15. The compound of claim 13, wherein A has an (S)-hydroxyl on the carbon atom alpha to the carbon atom linking A to the ring containing G.

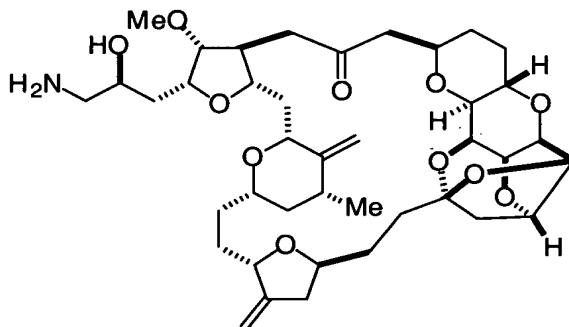
16. The compound of claim 6, wherein A comprises a C₁₋₆ saturated hydrocarbon skeleton having at least one substituent selected from hydroxyl and cyano.

17. The compound of claim 6, wherein Q₁ is independently selected from OR₁, SR₁, SO₂R₁, and OSO₂R₁ where each R₁ is independently selected from C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₆ aryl, C₆ haloaryl, C₁₋₃ alkoxy-C₆ aryl, C₆ aryl-C₁₋₃ alkyl, C₁₋₃ alkyl-C₆ aryl, C₆ haloaryl-C₁₋₃ alkyl, C₁₋₃ alkyl-C₆ haloaryl, and (C₁₋₃ alkoxy-C₆ aryl)-C₁₋₃ alkyl.

18. The compound of the following structure



19. The compound of the following structure



and pharmaceutically acceptable salts thereof.

20. A method for identifying an agent that induces a sustained mitotic block in a cell after transient exposure of said cell to said agent, said method comprising the steps of:

(a) incubating a first cell sample with a predetermined concentration of a test compound for a time interval between that sufficient to empty the G_1 population and that equivalent to one cell cycle;

(b) substantially separating said test compound from said first cell sample;

(c) incubating said first sample in media free of said test compound for a time interval sufficient to allow at least 80% of the cells released from the mitotic block induced by a highly reversible mitotic inhibitor to complete mitosis and return to the G_1 phase; and

(d) measuring the percentage of transiently-exposed cells from step (c) that have completed mitosis and returned to the G_1 phase.

21. The method of claim 20, further comprising the steps of:

(e) incubating a second sample of cells with a concentration of said test compound less than or equal to that used in step (a) for a time interval between that sufficient to empty the G₁ population and that equivalent to one cell cycle;

5 (f) measuring the percentage of cells from step (e) that have completed mitosis and have returned to the G₁ phase; and

(g) determining the relative reversibility of said test compound by relating the measurement of step (d) and the measurement of step (f).

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